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IP

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/404,448	09/22/99	BYRNE	B 4300.012100

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EXAMINER	
LEFFERS JR,G	
ART UNIT	**PAPER NUMBER**
1636	8

DATE MAILED: 07/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/404,448	Byrne, et al.
Examiner	**Group Art Unit**
Gerald G. Leffers Jr.	1636

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-27* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4 & 6*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Acknowledgment is made of applicants' amendment file 6/19/00 (Paper No. 7) in which applicants canceled the non-elected claims, 29-41. It is noted that the claims pending in the instant application are claims 1-17 and 19-28, as there was no claim 18 filed in the original application.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the citizenship for Barry Byrne is missing.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

As noted above, claim 18 is missing from the original specification. Misnumbered claims 19-41 have been renumbered as claims 18-40.

Double Patenting

Claim 6 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 4. Both claims are directed towards a recombinant HSV viruse comprising an AAV rep gene operably linked to a promoter, an AAV cap gene operably linked to a promoter and HSV ori/pac sequences (implied in claim 6). When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 23 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The application discloses a recombinant HSV-1/AAV hybrid virus (d27.1rc HSV-1) which is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed

invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-10 and 20-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite in that it is not clear as to what is intended by the phrase "altered to increase expression". Is the limitation of increased expression meant for the altered gene or for some other gene present in the recombinant vector (e.g. rep or cap)? Upon reading the specification it appears applicants may mean the limitation to refer to the level of expression for the altered gene itself. It would be remedial to amend the claim language such that it is clear as to which gene is to be expressed at a higher level as a result of the altered gene.

Claims 20 and 24 are vague and indefinite in that the metes and bounds of the term "suitable container" are unclear. What criteria are supposed to be used in order to determine if a container is a "suitable" container? The term is inherently indefinite and should be dropped from the claims as it adds nothing to the claims.

Claim 22 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said HSV-1 helper virus" in claim 21, upon which claim 23 is dependent.

Claim 23 is vague and indefinite in that it recites the limitation of an HSV-1 helper virus designated as "d27.1 HSV-1". It appears from reading the specification that the claimed virus is actually intended to be "d27.1rc HSV-1" and it would be remedial to amend the claim language accordingly.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 11-12, 15-17, 18, 20-22 and 224-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Dong et al (B1).

Dong et al teach the construction of helper viruses for production of rAAV which comprise genes essential for AAV replication (Abstract). Dong et al teach that the helper viruses of their invention can be derived from adenovirus or one of several different types of viruses classified in a general class of "herpesvirus", including HSV (page 6, lines 16-28). Dong et al teach that these helper viruses can either be replication competent (i.e. comprising viral packaging and origin of replication sequences) or replication defective (page 15, lines 19-29). Dong et al specifically teach that the herpesvirus helper viruses of their invention will, generally

speaking , comprise one or more of the AAV rep, lip and cap genes (page 7, lines 8-20). Dong et al teach that the essential AAV genes can be inserted into the helper virus genome at positions where either essential or non-essential genes from the helper virus genome have been deleted (page 7, lines 21-32). Dong et al teach that the helper viruses of their invention can promote the expression of the essential AAV genes with either "natural" AAV promoters (e.g. p5 from AAV) or heterologous promoters (page 8, lines 20-27; page 9, lines 4-14).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 11-12, 15-17 and 20-22 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dong et al (B1) in view of Chiorini et al (A).

The teachings of Dong et al are described above and are applied as before, except:

Dong et al do not explicitly teach the use of the p19 or p40 promoters.

Chiorini et al teach the use of a vector system comprising two vectors (a first rAAV vector and a second vector comprising an inducible origin of replication as well as sequences for expression of AAV rep and cap) for the production of rAAV virus particles (Abstract). Chiorini et al teach that the expression of the AAV rep and cap genes from the vectors of their system is under control of a suitable promoter, such as the AAV p5, p19 and p40 promoters (column 2, paragraph 2).

It would have been obvious to one of ordinary skill in the art to construct the helper viruses taught by Dong et al to include the use of p19 or p40 promoters operatively linked to one or both of the AAV rep or cap genes because Dong et al teach that any "natural" or heterologous promoters known in the art (including p5) could be used in their invention to drive transcription of the essential AAV genes and because Chiorini et al teach that the p5, p19 and p40 promoters are suitable for driving the expression of rep and cap coding sequences in a rAAV production system. One would have been motivated to do so in order to receive the expected benefit of providing expression of the desired gene products at different levels depending on the relative strength of the different promoters for the production of different rAAVs. Absent any evidence to the contrary, there would have been a reasonable expectation of success in utilizing the p19 or

p40 promoter to drive transcription of one or both of the cap and rep genes from one of the HSV helper constructs taught by Dong et al.

Claims 1-8, 11-12, 15-17, 18, 20-22 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dong et al (B1) and Glorioso et al (B).

The teachings of Dong et al are described above and applied as before, except:

Dong et al do not explicitly teach the alteration or deletion of the ICP27 or glycoprotein H genes for there HSV-1/AAV hybrid helper virus or vectors.

Glorioso et al teach the construction and use of a variety of HSV vectors (Abstract). Glorioso et al teach that the HSV genome is well characterized and that one can make deletion mutations in essential genes (in particular ICP4 & ICP27) such that the HSV vector is replication-defective unless grown in a host cell providing the missing translation product or products (column 2, paragraph 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the recombinant HSV vector taught by Dong et al to include a deletion of at least part of the ICP27 gene because Dong et al teach that it is within the skill in the art to make the helper-virus constructs of their invention comprising deletions of any non-essential or essential gene (e.g. glypcoprotein H or ICP27) so long as the essential gene products are provided in trans during replication of the helper virus and because Glorioso et al specifically teach that it is possible and desirable to make recombinant HSV vectors comprising a deletion of at least a

portion of the ICP27 gene. One would have been motivated to do so in order to receive the expected benefit of limiting the induction of herpesviral replication during the methods taught by Dong et al for production of rAAV with the HSV-helper vector. Absent any evidence to the contrary there would have been a reasonable expectation of success in incorporating a deletion in the ICP27 gene, as taught by Glorioso et al, in the recombinant HSV vectors taught by Dong et al for expression of AAV rep and cap during production of high-titre rAAV stocks.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GGL

G. Leffers, Jr.

Patent Examiner

Art Unit 1636

July 3, 2000

TERRY MCKELVEY
PRIMARY EXAMINER

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL ATTACHMENT

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.